STIC-Biotech/ChemLib

Fr m: Chan, Christina
Sent: Monday, September 09, 2002 1:40 PM
To: Nguyen, Quang (AU1632); STIC-Biotech/ChemLib
Subject: RE: RUSH sequence search request for 09/880887

Please rush. Thanks Chris

-----Original Message-----
From: Nguyen, Quang (AU1632)
Sent: Monday, September 09, 2002 1:38 PM
To: Chan, Christina
Subject: RUSH sequence search request for 09/880887

Good afternoon,

I would like to request a RUSH sequence search for the above special case.

Please search: SEQ ID NO:9

against commercial, issued US and pending application databases.

I am in AU 1636, CM1-12A12; my mailbox is in 11E12.

THANK YOU.

Point of Contact:
Susan Hanley
Technical Info. Specialist
CM1 6B05 Tel: 305-4053

Searcher: _____
Phone: _____
Location: _____
Date Picked Up: _____
Date Completed: _____
Searcher Prep/Review: _____
Clerical: _____
Online time: _____

TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST (where applic.)
STN: _____
DIALOG: _____
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: _____
Other (specify): _____

```
          140450  INSERT
             281  INTRON(W)INSERTION
          414637  MODIFIED
          191849  VECTOR
          167686  PLASMID
          245524  CDNA
             398  MODIFIED(W)((VECTOR OR PLASMID) OR CDNA)
      S6       0  (INTRON (W) INSERTION) AND (MODIFIED (W) (VECTOR OR
                  PLASMID OR CDNA))
?ds

Set     Items   Description
S1         14   (FACTOR (W) IX) (S) (INTRON (W) I)
S2          8   RD (unique items)
S3          5   (FACTOR (W) VIII) AND S2
S4          5   RD (unique items)
S5          1   (MODIFIED (W) CDNA) (S) (INTRON)
S6          0   (INTRON (W) INSERTION) AND (MODIFIED (W) (VECTOR OR PLASMID
              OR CDNA))
?logoff
       12sep02 11:58:14 User259876 Session D400.2
            $1.56    0.487 DialUnits File155
               $1.26  6 Type(s) in Format  3
            $1.26  6 Types
     $2.82  Estimated cost File155
            $2.85    0.510 DialUnits File5
              $14.00  8 Type(s) in Format  3
           $14.00  8 Types
    $16.85  Estimated cost File5
            $5.19    0.577 DialUnits File73
     $5.19  Estimated cost File73
            OneSearch, 3 files,  1.573 DialUnits FileOS
     $1.30  TELNET
    $26.16  Estimated cost this search
    $26.56  Estimated total session cost   1.672 DialUnits


### Status: Signed Off. (7 minutes)
```

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### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 02.08.23D

Last logoff:  11sep02 14:03:15
Logon file001 12sep02 11:52:05
           *** ANNOUNCEMENT ***
                    ***
--File 515 D&B Dun's Electronic Business Directory is now online
completely updated and redesigned. For details, see HELP NEWS 515.
                    ***
--File 990 - NewsRoom now contains May 2002 to present records.
File 993 - NewsRoom archive contains 2002 records from January 2002-
April 2002. To search all 2002 records, BEGIN 990,993 or B NEWS2002.
                    ***
--Alerts have been enhanced to allow a single Alert profile to be
stored and run against multiple files. Duplicate removal is available
across files and for up to 12 months. The Alert may be run according
to the file's update frequency or according to a custom
calendar-based schedule. There are no additional prices for these
enhanced features. See HELP ALERT for more information.
                    ***
--U.S. Patents Fulltext (File 654) has been redesigned with
new search and display features.  See HELP NEWS 654 for
information.
                    ***
--Connect Time joins DialUnits as pricing
options on Dialog.  See HELP CONNECT for
information.
                    ***
--CLAIMS/US Patents (Files 340,341, 942) have been enhanced
with both application and grant publication level in a
single record.  See HELP NEWS 340 for information.
                    ***
--SourceOne patents are now delivered to your
email inbox as PDF replacing TIFF delivery.
See HELP SOURCE1 for more information.
                    ***
--Important news for public and academic
libraries.  See HELP LIBRARY for more information.
                    ***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
                    ***
For information about the access to file 43 please see Help News43.
***
NEW FILES RELEASED
***Dialog NewsRoom - Current 3-4 months (File 990)
***Dialog NewsRoom - 2002 Archive (File 993)
***Dialog NewsRoom - 2001 Archive (File 994)
***Dialog NewsRoom - 2000 Archive (File 995)
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***TRADEMARKSCAN-Finland   ile 679)
***TRADEMARKSCAN-Norway  (File 678)
***TRADEMARKSCAN-Sweden  (File 675)
                    ***
UPDATING RESUMED
***Delphes European Business (File 481)
                    ***
RELOADED
***D&B Dun's Electronic Business Directory (File 515)
***U.S. Patents Fulltext 1976-current (File 654)
***Population Demographics (File 581)
***Kompass Western Europe (File 590)
***D&B - Dun's Market Identifiers  (File 516)
***PsycINFO (File 11)

REMOVED
***Chicago Tribune (File 632)
***Fort Lauderdale Sun Sentinel (File 497)
***The Orlando Sentinel (File 705)
***Newport News Daily Press (File 747)
***U.S. Patents Fulltext 1980-1989 (File 653)
***Washington Post (File 146)
***Books in Print (File 470)
***Court Filings (File 793)
***Microcomputer Software Guide Online (File 278)
***Publishers, Distributors & Wholesalers of the U.S. (File 450)
***State Tax Today (File 791)
***Tax Notes Today (File 790)
***Worldwide Tax Daily (File 792)

***New document supplier***
IMED has been changed to INFOTRIE (see HELP OINFOTRI)


     >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
     >>>    of new databases, price changes, etc.      <<<
                    ****
KWIC is set to 50.
HILIGHT set on as '*'
***                                    ***

File   1:ERIC  1966-2002/Sep 11
       (c) format only 2002 The Dialog Corporation

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?b 155, 5, 73
       12sep02 11:52:21 User259876 Session D400.1
            $0.35    0.099 DialUnits File1
     $0.35  Estimated cost File1
     $0.05  TELNET
     $0.40  Estimated cost this search
     $0.40  Estimated total session cost   0.099 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Sep W2
*File 155: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File   5:Biosis Previews(R)  1969-2002/Sep W1
         (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  73:EMBASE  1974-2002/Sep W1
         (c) 2002 Elsevier Science B.V.
```

***File 73: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.

```
      Set  Items  Description
      ---  -----  -----------
?s (factor (w) IX) (s) (intron (w) I)
         1833641  FACTOR
           36380  IX
           55981  INTRON
         2414603  I
      S1      14  (FACTOR (W) IX) (S) (INTRON (W) I)
?rd
...completed examining records
      S2       8  RD (unique items)
?t s2/3,k/all
```

2/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13427031 21412779 PMID: 11522009
A factor VIII minigene comprising the truncated *intron* *I* of *factor* *IX* highly improves the in vitro production of factor VIII.
Plantier J L; Rodriguez M H; Enjolras N; Attali O; Negrier C
INSERM U331, Laboratoire d'Hemobiologie-Faculte de Medecine RTH Laennec, Lyon, France.
Thrombosis and haemostasis (Germany) Aug 2001, 86 (2) p596-603, ISSN 0340-6245 Journal Code: 7608063
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A factor VIII minigene comprising the truncated *intron* *I* of *factor* *IX* highly improves the in vitro production of factor VIII.
The biosynthesis of coagulation factor VIII (FVIII) is hampered by successive controls that limit its production. To improve this production, a truncated *intron* *I* sequence of *factor* *IX* (TFIXI1). was inserted in FVIII cDNA in place of FVIII introns 1, 12 and 13 and also as a combination between introns 1 and 12...

2/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11254542 21290348 PMID: 11396323
Carrier detection and prenatal diagnosis in families with haemophilia.
Shetty S; Ghosh K; Bhide A; Mohanty D
Institute of Immunohaematology (ICMR), 13 Floor, New Multistoreyed Building, KEM Hospital, Parel, Mumbai 400012, Maharashtra, India.
National medical journal of India (India) Mar-Apr 2001, 14 (2) p81-3 , ISSN 0970-258X Journal Code: 8809315
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... genes. The polymorphisms used were intron 18 Bcl I, intron 19 Hind III, intron 22 Xbal and DXS52/St14 of the factor VIII gene and *intron* *I* Ddel, intron 4 Taql, 3 Hhal and Residue 148 codon Mnll of the *factor* *IX* gene. There were 189 probable carriers (whose carrier status was not known) and 99 obligatory carriers (confirmed carriers by family pedigree analysis) from 102 families...

2/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10492272 20010995 PMID: 10544911

The three in-frame ATG, clustered in the translation initiation sequence of human factor IX gene, are required for an optimal protein production.

Enjolras N; Rodriguez M H; Plantier J L; Maurice M; Attali O; Negrier C

INSERM U331, Laboratoire d'Hemobiologie-Faculte de Medecine RTH Laennec, Lyon, France.

Thrombosis and haemostasis (GERMANY) Oct 1999, 82 (4) p1264-9, ISSN 0340-6245 Journal Code: 7608063

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Three in-frame potential methionine codons have been identified in human *factor* *IX* gene and are clustered at amino acids -46, -41 and -39. In view of initiating a gene therapy approach, human *factor* *IX* production has been evaluated after modifications of these first three in-frame translation start sites. To characterize the most efficient translation initiation context, five *factor* *IX* cDNA expression vectors directed by CMV promoter-enhancer were generated. These vectors contained different starting site combinations including one, two or three ATG. A quantitative analysis of *factor* *IX* production in stably transfected CHO cells and in a rabbit reticulocyte lysate cell free system revealed the ability of all single site to generate fully active *factor* *IX*. However, the *factor* *IX* production level increased with the ATG number and the wild type (WT) cDNA bearing the 3 ATG induced the highest protein production. A truncated *intron* *I* of *factor* *IX* , previously suggested of having an expression-augmenting activity, was also placed in the WT *factor* *IX* cDNA. In stably transfected CHO cells, a 8-fold increase in protein production was measured. These results show that at least in vitro, the presence of the three ATG seems to be crucial for a maximal *factor* *IX* production. The data also suggest that both the three ATG and the truncated *intron* *I* are required for an optimal *factor* *IX* production in a perspective of a human gene therapy of haemophilia.

2/3,K/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08448930 95197522 PMID: 7890639

Role of *intron* *I* in expression of the human *factor* *IX* gene.

Kurachi S; Hitomi Y; Furukawa M; Kurachi K

Department of Human Genetics, University of Michigan Medical School, Ann Arbor 48109-0618.

Journal of biological chemistry (UNITED STATES) Mar 10 1995, 270 (10) p5276-81, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: HL38644; HL; NHLBI; M01-RR00042; RR; NCRR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Role of *intron* *I* in expression of the human *factor* *IX* gene.

The first intron (*intron* *I*) of the human *factor* *IX* gene, which has been previously suggested of having an expression-augmenting activity, was systematically studied for its potential enhancer activity. When tested with the chloramphenicol acetyltransferase expression vector with a minimal *factor* *IX* promoter, subregions of *intron* *I* showed only marginal enhancing activities (1.7-1.9-fold enhancement at the highest). Smaller subregions encompassing nucleotides 5660-6350 of the intron sequence even ...

... suppression at the highest), while a cytomegalovirus enhancer sequence, which was used as the positive control, had a 7-fold enhancement. A set of three *factor* *IX* minigene expression vectors with the same *factor* *IX*

promoter were then constructed: p-416FIXc which contained the *factor* *IX* cDNA, p-416FIXm1 which contained the *factor* *IX* cDNA with a largely truncated *intron* *I*, and p-416FIXm2 which contained the *factor* *IX* cDNA with the *intron* *I* sequence further truncated. The p-416FIXm1 and p-416FIXm2 constructs showed 7-9-fold higher expression activities than p-416FIXc. The elevated *factor* *IX* antigen levels agreed well with the grossly elevated *factor* *IX* clotting activity and mRNA levels. These results indicate that the expression enhancing activity of *intron* *I* is not due to specific enhancer elements present in the intron subsequences, but is due to functional splicing sequences present in the precursor mRNAs produced from the minigene constructs containing *intron* *I*. By being efficiently assembled into spliceosome complexes, transcripts with splicing sequences may be better protected in the nucleus from random degradations than those without such...

2/3,K/5 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13632744 BIOSIS NO.: 200200261565
Generation of whey acidic protein promoter-human factor IX transgenic mice for studies of oral tolerance to human factor IX in neonatal Hemophilia B mice.
AUTHOR: Sabatino Denise E(a); Arruda Valder R(a); Liu Yi-Lin(a); Velander William H; High Katherine A(a)
AUTHOR ADDRESS: (a)Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA**USA
JOURNAL: Blood 98 (11 Part 1):p825a-826a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

GENE NAME: human F.IX gene (human *factor* *IX* gene) (Hominidae...

...*intron* *I*;

2/3,K/6 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13558103 BIOSIS NO.: 200200186924
High-level gene expression of human factor VIII in vivo was achieved by a liver-specific construct containing ApoE-HCR and a heterologous intron.
AUTHOR: Miao Carol H(a); Ye Xin(a); Thompson Arthur R(a)
AUTHOR ADDRESS: (a)Medicine, Puget Sound Blood Center, University of Washington, Seattle, WA**USA
JOURNAL: Blood 98 (11 Part 1):p425a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: contain 1) a hepatic locus control region from ApoE gene (ApoE-HCR), 2) a liver-specific alpha1-antitrypsin promoter (HP), 3) a 1.4kb truncated *factor* *IX* *intron* (*I*) or a synthetic minx intron (mI), followed by 4) a multiple cloning site for inserting cDNA sequences, and 5) a bovine growth hormone polyadenylation signal...

...or an intronic sequence, produced levels less than 0.05 mug/ml. These

results are in paralle ith those obtained from the hi expressing human *factor* *IX* plasmid, pBS-HCRHP-FIXIA, where the truncated first intron of *factor* *IX* was in its native position between exons 1 and 2 (Miao et al. (2001) Mol. Ther. 3, 947-57). Our data demonstrate that combination of ApoE-HCR and a heterologous intron, either a truncated human *factor* *IX* first intron or a synthetic minx intron inserted 5' to factor VIII cDNA can greatly enhance factor VIII gene expression in vivo. It will be...

2/3,K/7 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13114851 BIOSIS NO.: 200100322000
Novel method for human factor VIII packaging and expression: Dimerization of rAAV vectors.
AUTHOR: Chao Hengjun(a); Walsh Christopher E(a)
AUTHOR ADDRESS: (a)UNC Gene Therapy Center, University of North Carolina at Chapel Hill, Chapel Hill, NC**USA
JOURNAL: Blood 96 (11 Part 1):p216a-217a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

...ABSTRACT: sequence. The upstream or 5 vector included a enhancer/promoter cassette linked with a portion of the FVIII cDNA (exons 1-12) and the truncated *intron* *I* sequence of human *factor* *IX* carrying a splice donor site. The downstream or 3 vector contained an intronic sequence with a splice acceptor site linked to the remaining FVIII cDNA...

2/3,K/8 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12284528 BIOSIS NO.: 200000042395
A combination of truncated *factor* *IX* *intron* *I* highly improves FVIII production.
AUTHOR: Plantier J-L(a); Rodriguez M-H(a); Enjolras N(a); Rea M(a); Negrier C(a)
AUTHOR ADDRESS: (a)Laboratoire d'Hemobiologie, Faculte RTH Laennec, INSERM U331, Lyon**France
JOURNAL: Blood 94 (10 SUPPL. 1 PART 1):p454a Nov. 15, 1999
CONFERENCE/MEETING: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999
SPONSOR: The American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Citation
LANGUAGE: English

A combination of truncated *factor* *IX* *intron* *I* highly improves FVIII production.
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...*factor* *IX* *intron* *I*;
?ds

Set	Items	Description
S1	14	(FACTOR (W) IX) (S) (INTRON (W) I)
S2	8	RD (unique items)

?s (factor (w) VIII) and
1833641 FACTOR
52261 VIII
33931 FACTOR(W)VIII
8 S2
S3 5 (FACTOR (W) VIII) AND S2
?rd
...completed examining records
S4 5 RD (unique items)
?t s4/3,k/all

4/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13427031 21412779 PMID: 11522009
A *factor* *VIII* minigene comprising the truncated *intron* *I* of *factor* *IX* highly improves the in vitro production of *factor* *VIII*.
Plantier J L; Rodriguez M H; Enjolras N; Attali O; Negrier C
INSERM U331, Laboratoire d'Hemobiologie-Faculte de Medecine RTH Laennec, Lyon, France.
Thrombosis and haemostasis (Germany) Aug 2001, 86 (2) p596-603, ISSN 0340-6245 Journal Code: 7608063
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A *factor* *VIII* minigene comprising the truncated *intron* *I* of *factor* *IX* highly improves the in vitro production of *factor* *VIII*.
The biosynthesis of coagulation *factor* *VIII* (FVIII) is hampered by successive controls that limit its production. To improve this production, a truncated *intron* *I* sequence of *factor* *IX* (TFIXI1) was inserted in FVIII cDNA in place of FVIII introns 1, 12 and 13 and also as a combination between introns 1 and 12...
Descriptors: Factor IX--genetics--GE; **Factor* *VIII*--biosynthesis--BI; **Factor* *VIII*--genetics--GE; *Introns--genetics--GE
Chemical Name: Recombinant Fusion Proteins; Repressor Proteins; *Factor* *VIII*; Factor IX

4/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11254542 21290348 PMID: 11396323
Carrier detection and prenatal diagnosis in families with haemophilia.
Shetty S; Ghosh K; Bhide A; Mohanty D
Institute of Immunohaematology (ICMR), 13 Floor, New Multistoreyed Building, KEM Hospital, Parel, Mumbai 400012, Maharashtra, India.
National medical journal of India (India) Mar-Apr 2001, 14 (2) p81-3, ISSN 0970-258X Journal Code: 8809315
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... factors VIII and IX genes. The polymorphisms used were intron 18 Bcl I, intron 19 Hind III, intron 22 Xbal and DXS52/St14 of the *factor* *VIII* gene and *intron* *I* Ddel, intron 4 Taql, 3 Hhal and Residue 148 codon Mnll of the *factor* *IX* gene. There were 189 probable carriers (whose carrier status was not known) and 99 obligatory carriers (confirmed carriers by family pedigree analysis) from 102 families...

...and 63 as non-carriers by the intragenic polymorphic markers in families with haemophilia A. Eighteen women were informative with only the extragenic marker of *factor* *VIII* gene. Four women were not informative with any of the markers used. In families with haemophilia B, 37 women were

diagnosed as carriers and 4...
; Factor IX--genetics--GE; *Factor* *VIII*--genetics--GE; Linkage (Genetics); Mutation; Pedigree; Prenatal Diagnosis--methods--MT; X Chromosome
Chemical Name: *Factor* *VIII*; Factor IX

4/3,K/3 (Item 1 from file: 5)

13558103 BIOSIS NO.: 200200186924
High-level gene expression of human *factor* *VIII* in vivo was achieved by a liver-specific construct containing ApoE-HCR and a heterologous intron.
AUTHOR: Miao Carol H(a); Ye Xin(a); Thompson Arthur R(a)
AUTHOR ADDRESS: (a)Medicine, Puget Sound Blood Center, University of Washington, Seattle, WA**USA
JOURNAL: Blood 98 (11 Part 1):p425a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

High-level gene expression of human *factor* *VIII* in vivo was achieved by a liver-specific construct containing ApoE-HCR and a heterologous intron.

ABSTRACT: *Factor* *VIII* gene transfer has been problematic because of the large size of its cDNA and instability of the gene product. Gene expression of *factor* *VIII* was sometimes limited by endogenous transcriptional silencing sequences and other inhibition steps. Furthermore, *factor* *VIII* protein undergoes multiple post-transcriptional modifications before secretion, and is stabilized by binding to von Willebrand factor in the circulation before activation. To ensure correct modification and protection of the synthesized protein, the liver which is the major native site for *factor* *VIII* biosynthesis is considered a preferential site for gene transfer of *factor* *VIII*. Recently we have developed two nonviral gene transfer vectors for high-level gene expression in the liver. The expression cassettes contain 1) a hepatic locus control region from ApoE gene (ApoE-HCR), 2) a liver-specific alpha1-antitrypsin promoter (HP), 3) a 1.4kb truncated *factor* *IX* *intron* (*I*) or a synthetic minx intron (mI), followed by 4) a multiple cloning site for inserting cDNA sequences, and 5) a bovine growth hormone polyadenylation signal (A) to make pBS-HCRHPI-A or pBS-HCRHPmI-A. A B-domain deleted *factor* *VIII* cDNA was inserted into the multiple cloning sites of these two vectors. One day after rapid injection of 50 mug of the constructs, pBS-HCRHPI...

...into the tail vein of mice (n=6/each group), range of 2-25.5 mug/ml and 0.7-5 mug/ml of human *factor* *VIII* circulated, respectively (normal=0.1mug/ml in human plasma). A control plasmid, pBS-HP-FVIIIA, without the ApoE-HCR or an intronic sequence, produced levels less than 0.05 mug/ml. These results are in parallel with those obtained from the high expressing human *factor* *IX* plasmid, pBS-HCRHP-FIXIA, where the truncated first intron of *factor* *IX* was in its native position between exons 1 and 2 (Miao et al. (2001) Mol. Ther. 3, 947-57). Our data demonstrate that combination of ApoE-HCR and a heterologous intron, either a truncated human *factor* *IX* first intron or a synthetic minx intron inserted 5' to *factor* *VIII* cDNA can greatly enhance *factor* *VIII* gene expression in vivo. It will be of interest to investigate whether the expression can be further enhanced by inserting a heterologous intron or *factor* *VIII* introns into different positions in the vector. Furthermore, the liver-specific vectors can be used to deliver heterologous genes for high-level transgene expression. These high-expressing human *factor* *VIII* cassettes can be readily inserted

into viral or nonviral [redacted]ctors for achieving effective g[redacted]e therapy of hemophilia A.
...REGISTRY NUMBERS: *FACTOR* *VIII*; ...

...*FACTOR* *VIII*; ...

...*FACTOR* *VIII*
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...*factor* *VIII*--...
...*factor* *VIII* cDNA {*factor* *VIII* complementary DNA
...GENE NAME: human *factor* *VIII* gene (Hominidae...

4/3,K/4 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13114851 BIOSIS NO.: 200100322000
Novel method for human *factor* *VIII* packaging and expression: Dimerization of rAAV vectors.
AUTHOR: Chao Hengjun(a); Walsh Christopher E(a)
AUTHOR ADDRESS: (a)UNC Gene Therapy Center, University of North Carolina at Chapel Hill, Chapel Hill, NC**USA
JOURNAL: Blood 96 (11 Part 1):p216a-217a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

Novel method for human *factor* *VIII* packaging and expression: Dimerization of rAAV vectors.

ABSTRACT: Hemophilia A is an x-linked hemorrhagic disease due to deficiency in coagulation *factor* *VIII* (FVIII). Gene therapy offers a promising approach to treat genetic diseases like hemophilia A. Recombinant adeno-associated virus (rAAV) has attracted significant interest due to its non-pathogenicity, and its capability to transduce liver and persist. A major obstacle in the application of rAAV for *factor* *VIII* gene transfer is the vectors limited packaging capacity (apprx5.0 kb) and large size of the FVIII cDNA (7 kb). In our previous study (Chao...

...sequence. The upstream or 5 vector included a enhancer/promoter cassette linked with a portion of the FVIII cDNA (exons 1-12) and the truncated *intron* *I* sequence of human *factor* *IX* carrying a splice donor site. The downstream or 3 vector contained an intronic sequence with a splice acceptor site linked to the remaining FVIII cDNA...
...REGISTRY NUMBERS: *FACTOR* *VIII*; ...

...*FACTOR* *VIII*; ...

...*FACTOR* *VIII*
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...*factor* *VIII*--

4/3,K/5 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12284528 BIOSIS NO.: 200000042395
A combination of truncated *factor* *IX* *intron* *I* highly improves FVIII production.

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JOURNAL: Blood 94 (10 SUPPL. 1 PART 1):p454a Nov. 15, 1999
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LANGUAGE: English

A combination of truncated *factor* *IX* *intron* *I* highly improves FVIII production.
...REGISTRY NUMBERS: *FACTOR* *VIII*; ...

...*FACTOR* *VIII*; ...
...*FACTOR* *VIII*
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...*factor* *IX* *intron* *I*; *factor* *VIII*--
?ds

Set	Items	Description
S1	14	(FACTOR (W) IX) (S) (INTRON (W) I)
S2	8	RD (unique items)
S3	5	(FACTOR (W) VIII) AND S2
S4	5	RD (unique items)

?s (modified (w) cDNA) (s) (intron)

	414637	MODIFIED
	245524	CDNA
	55981	INTRON
S5	1	(MODIFIED (W) CDNA) (S) (INTRON)

?t s5/3,k/all

5/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13104882 BIOSIS NO.: 200100312031
Characterization of genes regulated by PU.1.
AUTHOR: Nelson Stacy L(a); Torbett Bruce E; Klemsz Michael J(a)
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JOURNAL: Blood 96 (11 Part 1):p672a-673a November 16, 2000
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ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

...ABSTRACT: in myeloid cells. Little is known, however, about genes regulated by PU.1 in myeloid precursor cells. To address this question, we have used two *modified* *cDNA* subtraction techniques to identify genes differentially expressed in the myeloid cell lines, 503 and 503PU. The 503 cell line is an IL-3 dependent line...
...does not regulate SLPI expression through this sequence. We are now assessing whether PU.1 regulates SLPI expression through potential PU.1 sites located within *intron* 2, or through the regulation of other transcription factors. The second cDNA subtraction method used combines RDA followed by a differential cDNA library screen. The...
?s (intron (w) insertion) and (modified (w) (vector or plasmid or cDNA))

	55981	INTRON